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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/250,056	02/12/1999	JAMES D. MARKS	2307E-852	1647

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EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 03/17/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/250,056

Applicant(s)

MARKS ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-22,34-44,53 and 54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-13,16-22,34-44,53 and 54 is/are rejected.
- 7) ☒ Claim(s) 14 and 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. NOTE: This application requested for an RCE by the paper filed 12/31/02 and marked the "amendment/reply" box and also submitted 12/31/02 was an IDS, however, the IDS box on the RCE form was not marked. A telephone call was placed on 1/15 to Mr. Hunter to check if an amendment was filed in addition to the IDS. Mr. Hunter stated that no amendment was filed only an IDS. The Examiner noted that no 1449 was supplied and the references will be placed on a PTO-892.

Request for Continued Examination

2. The request filed on 12/31/02 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/250,056 is acceptable and a RCE has been established. Claims 1, 3-22, 34-44, 53-54 are pending and are currently under prosecution. An action on the RCE follows.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

4. It is noted that the RCE filed 12/31/02 did not contain an amendment or a reply as stated above. The RCE did not address any of the rejections by amendment or response.

Oath/Declaration

5. The Examiner acknowledges that a new oath is being executed, however, he oath or declaration is still defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is still defective because:

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment [emphasis added] specifically referred to in the oath or declaration.

Rejections Withdrawn

6. The rejection of claims 3, 5, 21-22, 43-44 under 35 U.S.C. 112, first paragraph, is withdrawn upon further consideration.

7. The rejection of Claims 14, 15, under 35 U.S.C. 103(a) as being unpatentable over Maier et al (Cancer Res. 51:5361-5369, 1991) and further in view of Bird et al (Science 242:423-426, 1988) is withdrawn upon further consideration since Maier does not teach a single chain antibody of SEQ ID NO:1 or 2.

8. The rejection of Claims 1, 34-38, and 53-54 under 35 U.S.C. 103(a) as being unpatentable over Maier et al (Cancer Res. 51:5361-5369, 1991) and further in view of Bird et al (Science 242:423-426, 1988) is withdrawn in view of the new grounds of rejections.

Response to Arguments

9. The rejection of claims 3-13, 16-20, 34-42, and 53-54, under 35 U.S.C. 112, first paragraph, is maintained.

The response filed 12/31/02 has been carefully considered but has been deemed to be not persuasive. The response did not address this rejection. The claims still encompass antibodies with conservative substitutions, 70% identity and affinity of only 10mM, and antibodies with no more than 30 residue differences wherein the alterations, substitutions, or differences can be in the CDRS. The claims encompass antibodies with one, two, or three CDRS from SEQ ID NO:1 or 2 and any CDRs from any other molecule and claim 16 which is not clear at all (see 112 second rejection below) which encompasses antibodies which don't bind the same epitope as SEQ ID NO:1 or 2. Therefore, the rejection is maintained.

The following are some NEW GROUNDS of rejection

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 16-22, 34-44, 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 and those that depend from claim 16 are indefinite because it is not clear what applicant is claiming in claim 16. The claim recites a single chain that binds to C-erbB2 receptor and comprises any 10 contiguous amino acids of SEQ ID NO:1 or 2 wherein the antibody elicits an anti-id that binds to SEQ ID NO:1 or 2 and does not bind antisera raised against SEQ ID NO:1 or 2 that has been fully immunosorbed with SEQ ID NO:1 or 2. It is not clear if the single chain binds the same epitope as the antibodies of SEQ ID NO:1 or 2 or if the antibody mimics the epitope. Applicants are invited to clarify claim 16.

Claim Rejections - 35 USC § 103

12. Claims 1, 34-38, 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al (int. J. Cancer 53:401-8, 1993) and further in view of Bird et al (Science 242:423-426, 1988, PTO-892 part of #15) and Chaudhary et al (PNAS 87:1066-70, 1990).

The claims recite a single chain antibody that binds to the same epitope as F5 or C1 and is internalizing, a chimeric comprising a cytotoxin and compositions comprising such.

Xu et al teach hybridomas and antibodies produced from such that are internalizing and bind to c-erbB2. Xu et al does not teach a single chain or an immunotoxin. These deficiencies are made up for in the teachings of Bird et al and Chaudhary et al.

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Bird teach single chain antibodies.

Chaudhary teach single chain immunotoxins.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Xu et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Xu et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Bird et al teach "Single chain antigen binding proteins are expected to have advantages in clinical applications because of their small size" (see page 426) and because Chaudhary et al teach the method is rapid and one can obtain the VH and VL genes from PCR and the immunotoxins can be used directly as fusion proteins and domain I of PE promotes internalization (see page 1069). In addition, One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Xu et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Xu et al teach ricin A conjugates (which are immunotoxin conjugates) can exert different levels of cytotoxicity (see page 407).

It is the Examiner's position that Xu et al have produced an antibody that has the same properties as claimed which are binding to the same epitope as F5 or C1 and is internalized recited in the claims. One of ordinary skill in the art would reasonably

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conclude that Xu et al's antibody also possesses the same properties as claimed and, therefore, it appears that Xu et al have produced an antibody that is identical to the claimed antibody. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Xu et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

13. Claims 1, 34-38, 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maier et al (Cancer Res 51:5361-5369, 1991) and further in view of Bird et al (Science 242:423-426, 1988, PTO-892 part of #15) and Chaudhary et al (PNAS 87:1066-70, 1990).

The claims have been described supra.

Maier et al teach hybridomas and antibodies produced from such that are internalizing and bind to c-erbB2. Maier et al does not teach a single chain or an immunotoxin. These deficiencies are made up for in the teachings of Bird et al and Chaudhary et al.

Bird teach single chain antibodies.

Chaudhary teach single chain immunotoxins.

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It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Maier et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Maier et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Bird et al teach "Single chain antigen binding proteins are expected to have advantages in clinical applications because of their small size" (see page 426) and because Chaudhary et al teach the method is rapid and one can obtain the VH and VL genes from PCR and the immunotoxins can be used directly as fusion proteins and domain I of PE promotes internalization (see page 1069). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Maier et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Maier et al teach radiolabelled conjugates and immunoconjugates of the antibody and ricin.

It is the Examiner's position that Maier et al have produced an antibody that has the same properties as claimed which are binding to the same epitope as F5 or C1 and is internalized recited in the claims. One of ordinary skill in the art would reasonably conclude that Maier et al's antibody also possesses the same properties as claimed and, therefore, it appears that Maier et al have produced an antibody that is identical to the claimed antibody. Since the Patent and Trademark Office does not have the

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facilities for examining and comparing the claimed antibody with the antibody of Maier et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

14. Claims 1, 34-38, 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shawver et al (Cancer Res 54:1367-1373, 1994) and further in view of Bird et al (Science 242:423-426, 1988, PTO-892 part of #15) and Chaudhary et al (PNAS 87:1066-70, 1990).

The claims have been described supra.

Shawver et al teach hybridomas and antibodies produced from such that are internalizing and bind to c-erbB2 and labeled antibodies. Shawver et al does not teach a single chain or an immunotoxin. These deficiencies are made up for in the teachings of Bird et al and Chaudhary et al.

Bird teach single chain antibodies.

Chaudhary teach single chain immunotoxins.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Shawver et al and

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produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Shawver et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Bird et al teach "Single chain antigen binding proteins are expected to have advantages in clinical applications because of their small size" (see page 426) and because Chaudhary et al teach the method is rapid and one can obtain the VH and VL genes from PCR and the immunotoxins can be used directly as fusion proteins and domain I of PE promotes internalization (see page 1069). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Shawver et al and produce a single chain or a single chain immunotoxin as taught by Bird et al and Chaudhary et al because Shawver et al teach radiolabeled conjugates of the antibody.

It is the Examiner's position that Shawver et al have produced an antibody that has the same properties as claimed which are binding to the same epitope as F5 or C1 and is internalized recited in the claims. One of ordinary skill in the art would reasonably conclude that Shawver et al's antibody also possesses the same properties as claimed and, therefore, it appears that Shawver et al have produced an antibody that is identical to the claimed antibody. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Shawver et al, the burden of proof is upon the Applicants to show an unobvious

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distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Summary

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

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Larry R. Helms Ph.D.

A handwritten signature in black ink, appearing to be 'L. Helms', written in a cursive style.